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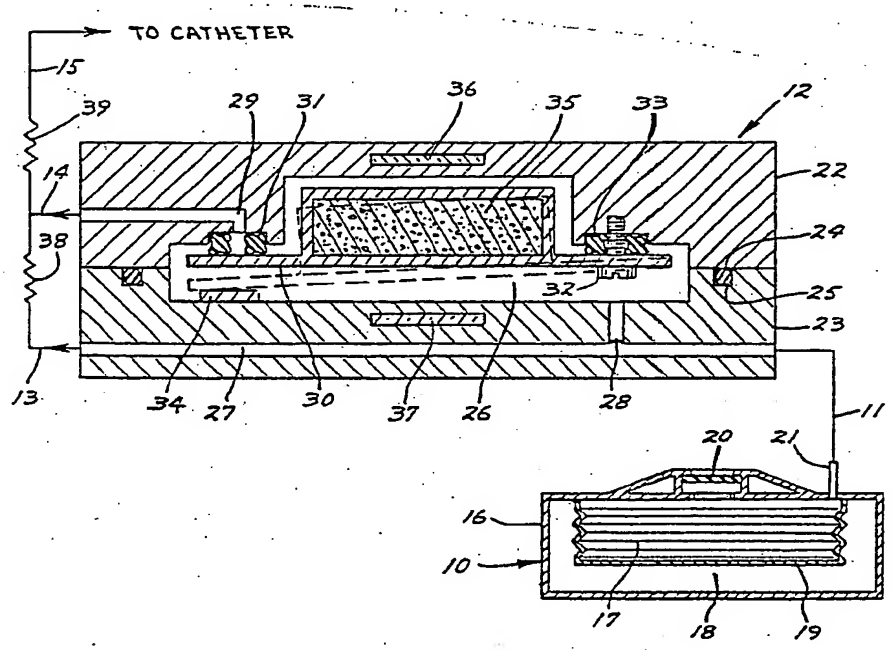
(54) Title: MAGNETICALLY CONTROLLED DRUG INFUSION SYSTEM



(57) Abstract

A magnetically controlled valving system (12) for use with a pressurized drug storage chamber and delivery device (10) to permit administration of the stored drug at different flow rates. The valve includes a valving element (30) which is magnetically actuated between open and closed positions either by means of an external magnet or an implanted electromagnet (35). The valve may include magnetic biasing means (36, 37) to latch the valve element in either of its positions. The valve may be operated in either a manual or electronic mode. For safety, the electronic mode may be overridden by means of an external magnet.

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MAGNETICALLY CONTROLLED DRUG INFUSION SYSTEM

Technical Field

The present invention relates to the field of medical devices, more particularly, an accessory for controlling a drug infusion device.

Background of the Invention

This invention is directed to an accessory device for accurately controlling the flow rate of drugs from drug delivery devices that depend on a fluid restriction to limit the flow rate from a pressurized drug storage chamber. One device of this type is the implantable infusion pump illustrated and described in U. S. Patent No. 3,731,681, the disclosure of which is incorporated herein by reference. Specifically, the present invention is directed to a magnetically controlled valving system designed to permit variable flow rates dependent upon need while guarding against over-doses of drugs. The magnetically controlled valve is used to modulate the flow rate of drug delivered from the constant pressure source in the implanted infusion pump.

When an implanted infusion pump is used, for example, to deliver insulin for the treatment of diabetes, two different flow rates are desirable, ranging from a low of about 1 cc/day to a high of from about 10 to 15 cc/day. The high flow rate of this magnitude is needed to deliver insulin fast enough to compensate for the absorption of glucose from ingested meals, the function of the insulin being to keep the glucose level in the bloodstream within prescribed limits. Administration of insulin at high levels could be fatal if continued for any substantial period of time after the glucose absorption is completed. Even the delivery of what would be a normal high dose of

insulin after a meal would be harmful if for some reason that meal was not absorbed normally, due to vomiting, for example. Another hazard would arise in the event of mechanical failure of some component in the pump permitting the stored dose of insulin, which is intended to last for at least one month, to be released too rapidly for the body to use. These hazards are compounded by the fact that the periodic high flow rate needed for proper therapy is above the body tolerance if sustained for too long a period of time.

Use of the implantable drug infusion pump of U. S. Patent No. 3,731,681 has been largely limited to situations calling for a continuous infusion rate, such as heparinization. Use for treatment of insulin, for example, has been handicapped by inability to dispense a drug, insulin in this instance, at different infusion rates. Although some efforts have been made toward providing different flow rates wholly by implanted electronic means, inherent problems remain due to unanticipated situations of use. The earliest form of the present invention is described in a paper by the present inventor and his co-workers (Perkins et al: Design and Initial Testing of a Totally Implantable Transcutaneously Controllable Insulin Delivery Device, Trans. Am. Soc. Artif. Intern. Organs, Vol. IV, pp 229-31, 1978) incorporated herein by reference.

Summary of the Invention

The present invention is directed to an implantable magnetically controlled system for the infusion of drugs into an animal body from a pressure actuated drug delivery device. Although the system may be electronically controlled, the electronic control may be overridden by an external magnet, or the system may be wholly controlled by an external magnet. The system includes a magnetically actuated valve disposed between the drug storage and pump device and a catheter extending to the intended infusion site. The flow line includes restrictors of different re-

sistance to permit the selection of different infusion flow rates.

The valve includes a body having a shallow enclosed cavity with an inlet opening to one side and an outlet opening from the opposite side. A movable valving element is positioned within the cavity to obstruct one of these openings. A permanent armature magnet is associated with the valving element to permit it to be moved between an open and a closed position. Biasing means are provided within the body to maintain the valving element in one of these two positions relative to the obstructed opening. Preferably, the biasing means are one or two permanent biasing magnets or ferromagnetic shunts associated with the valve body and armature magnet so as to maintain the valving element normally in an open or closed position, as desired.

The valving element is preferably a flap disk hinged on one side and adapted to obstruct one of the openings, preferably the outlet, into the cavity. A bypass passage is provided, preferably through the valve body and in communication with the inlet to the body cavity, to provide for a continuous low infusion rate as determined by a flow restrictor of high resistance. The valve outlet is connected to a restrictor of lesser resistance so that when the drug is delivered through the valve, a different and higher flow rate may be achieved. The valve may be activated magnetically either by means of a strong permanent magnet outside of the body held close to the implanted valve or by an internal implanted electromagnetic coil associated with the valve body and connected to an implanted power source through an appropriate control circuit.

Brief Description of the Drawings

The invention is illustrated in the accompanying drawings in which corresponding parts are identified by the same numerals and in which:

FIGURE 1 is a schematic representation of the implantable drug delivery system according to the present invention, showing the magnetically controllable valve in vertical section;

FIGURE 2 is a schematic of an electronic control system for the magnetically controllable valve;

FIGURE 3 is a schematic representation of the physical configuration of the drug delivery system in which the electronic control unit is in a separate but connected package; and

FIGURE 4 is a similar schematic of the system in which the electronic control package is mated to the pump and valve bodies.

Detailed Description of the Preferred Embodiment

Referring now to the drawings, and particularly to FIGURE 1, there is shown one form of pressure actuated drug delivery system, such as an implantable infusion pump, indicated generally at 10, connected through a drug flow line 11 to a magnetically controlled valve, indicated generally at 12. Valve 12 in turn is connected through flow lines 13, 14, and 15 to a catheter, not shown, leading to the desired infusion site. A preferred form of catheter is shown in my copending United States application Serial No. 29,640, filed 13 April, 1979.

The exemplary drug delivery device, implantable infusion pump 10, comprises a housing 16 divided into a drug chamber 17 and a propellant chamber 18 by means of a bellows diaphragm 19. The infusion pump is implanted in an animal under the skin surface so that the drug chamber may be replenished hypodermically through the skin and through a penetrable resilient stopper 20. The propellant chamber 18 contains a liquid whose vapor pressure is such that, under the conditions of normal body temperature, pressure is exerted upon the bellows to force the drug contained therein out through discharge opening 21 through the flow line 11 to the valve 12.

Valve 12 includes a body composed of mating upper and lower portions 22 and 23 fastened together as by welding, or by means of screws or equivalent fastening members. A resilient O-ring 24 is disposed in a recess 25 in the surface between the mating body members to seal the unit. The valve body encloses a shallow cavity 26, preferably circular, formed in the upper and lower body members. The valve body is preferably formed from titanium, which is inert and biocompatible. A bypass flow passage 27 preferably passing through the lower valve body member 23, connects flow lines 11 and 13. An inlet opening 28 is provided to valve cavity 26 to permit drug flow from the pump and flow line 11 through the valve. An outlet opening 29 from the valve cavity permits flow of drug from the valve to flow line 14.

A valving element in the form of a hinged disk 30 functions to open or close outlet opening 29. A resilient O-ring 31 is seated in a recess around the opening and engages the surface of valve disk 30 in insure a tight seal. Disk 30 is hinged adjacent its edge diametrically opposite from its engagement with the outlet opening, as by means of a screw 32 extending through an O-ring 33 into the cavity wall defined by the lower surface of upper valve body member 22. Valve disk 30 is preferably formed from titanium which is inert, biocompatible, and has a long flex life. A stop 34 may be provided to limit the movement of the disk.

Movement of valve disk 30 is controlled by a relatively large diameter (0.5 in.) permanently magnetic armature disk 35, preferably of samarium-cobalt. The armature magnet 35 is preferably sealed within a thin walled titanium shell forming part of the valve disk, as illustrated. Although the valve disk might be spring biased into either open or closed position, preferably biasing is accomplished by means of further magnetic biasing means such as permanent smaller magnetic disks or ferromagnetic shunt plates 36 and 37 to bias the valve

disk in the desired position. The biasing magnets are preferably of samarium-cobalt having fields of intensity equal to or preferably less than the field of the armature magnet and with their magnetic axes in substantial alignment. The force of attraction between the armature magnet and the biasing magnets is proportional to the area of the pole divided by the distance to the third power. Accordingly, by adjustment of the distance of each magnet or shunt from the armature magnet, the armature can be made to latch in either open or closed state or can be set to give any ratio of opening to holding force when operated in a non-latching mode, as explained in greater detail hereinafter.

Bypass flow line 13 includes a capillary flow restrictor 38. Flow line 15, in series, includes a capillary flow restrictor 39 of lesser resistance. In the instance of insulin, the relative resistances of restrictors 38 and 39 may be in the ratio of 15 to 1. Thus, so long as the valve is closed, insulin bypassing the valve and subject to the greater resistance of restrictor 38 is infused at a low rate. When the valve is opened by magnetic action on the armature magnet 35 and the insulin flows through the valve through flow line 14 to the restrictor 39 of lesser resistance, then the drug is administered at a substantially higher rate.

The valve is adapted to be implanted within the body in close proximity to the skin surface with the magnetic axis of the armature magnet perpendicular to the body surface. The armature magnet reacts to the presence of another strong permanent magnet placed outside the body and aligned to the same axis, or to an electromagnet implanted adjacent to the valve body. The field can penetrate the body tissue and the housing of the control valve with no effect on either. If like poles are adjacent, the two magents will repel each other. If unlike poles are adjacent, the two magets will attract each other. The valve is preferably in a normally closed

position. To prevent accidental opening of the valve by the presence of ferromagnetic material outside the body, the repulsion mode is selected to open the valve and the attraction mode is used to hold the valve shut. Common iron or steel objects are attracted by the internal magnet and only increase the force holding the valve shut. Strong magnetic fields of the intensity needed to open the valve are not common objects that would be encountered outside of specialized technical areas.

When the pump is designed for activation solely by an external magnet, when that external magnet is brought up to the implanted pump and control valve, the repulsion force is felt and a distinct effort is needed to hold the magnet in place to maintain the valve "open" state. The reverse condition of valve "closing", however, attracts the external magnet and it will stay in place by itself. If for any reason the operator (patient) loses conscious control of the external magnet, it will tend to flip over to attract the valve into the safe closed state. Because of these tactile feedback efforts, the patient will know the state of the implanted control valve and can only administer an overdose of the drug by conscious effort.

Where one biasing permanent magnet or ferromagnetic shunt is used, it is so positioned and spaced to maintain the valve disk in normally closed position assisted by the spring force of the valve disk and fluid pressure of the drug within chamber 26 on the disk. The activating outside permanent magnet or implanted electromagnet must be strong enough to overcome these combined forces. The valve will remain open so long as the outside permanent magnet is held in place or the electromagnetic coil is energized.

Where a pair of small permanent magnets or ferromagnetic shunt plates are disposed on opposite sides of the armature magnet, the valve disk may also be latched into open position. The net force on the armature magnet

is the sum of the two opposing forces and the force between the armature and closest biasing magnet or shunt dominates. By adjustment of the distance of each magnet or shunt, the holding force in each direction can be set. These holding forces are set so that the stronger holding force maintains the valve in normally closed position. The valve now needs a large impulse of force to open, supplied by the external magnet or internal electromagnet. Once open, the much smaller holding force of the biasing means will keep it there.

Where the primary activation of the valve is from an internal implanted electromagnet, an external permanent magnet can be used to overpower the internal electromagnet to provide an override control function. If the external magnet is placed to pull on the armature, the electromagnet cannot exceed the combined pull of the internal bias magnet or shunt and the external control magnet. If the valve is already open, the external magnet can exceed the holding force of the bias magnet or shunt (or the electromagnet) and force the valve shut. If the electromagnet fails to operate to open the valve, the external magnet can be used to open the valve and hold it open as long as the magnet is held in place. If the electromagnet tries to impulse the valve shut, the external magnet will immediately reopen the valve or, if the magnet is strong enough, completely override the closing impulse.

As shown schematically in FIGURE 2, the electronic package may contain a circuit to generate a series of impulses to hold the valve open in a programmed sequence of time intervals. A clock circuit may supply timing impulses. The timing impulses may be stored in semi-conductor or other electronic memory circuits. The control circuit puts out a voltage to the amplifier which drives the electromagnetic coil located in the proximity of the valve. The program can be altered by controlled impulses delivered to the implanted control circuit from an external transmitter. The electromagnet can serve as a

telemetry antenna to pick up these control signals. The implanted electronic circuit may be as complex as needed to supply the correct delivery algorithm for the particular drug to be infused.

The electromagnetic coil is placed over the armature magnet outside the valve housing. The coil is wound as a flat spiral of several layers. The coil covers the region of high field intensity which is the size of the armature magnet. When current is sent through the coil, the magnetic field of the coil reacts with the field of the armature magnet to produce attraction or repulsion force, depending on the current flow direction. A larger current is needed to open the valve against the combined forces of the bias means, spring force and fluid pressure at the seal. Once open, a smaller current can hold the valve open. To insure prompt closing, a pulse of current in the reverse direction will provide the force to accelerate the armature to the closed condition. The coil is preferably enclosed in a thin titanium shell to reduce eddy currents from the changing magnetic field. The magnetic field penetrates the metal between the coil and the armature magnet with no losses other than from the spacing gap.

As seen in FIGURES 3 and 4, the control circuit may be housed in an electronic package 40 remote from the pump and valve and connected to the electromagnetic coil 41 through a flexible conductor conduit 42, or an electronic package 43 may be shaped to conform to and mate with the rest of the pump and the valve package and held in place using medical grade silastic cement. The magnetic valve may be combined with other elements into a flow control package external to the pump which supplies a constant source of pressurized drug. That package may include the flow restrictors and a flow control regulator, as described and claimed in my copending United States application Serial No. 35,535, filed 3 May, 1979. An auxiliary septum 44 may be provided connected to the out-

let to the catheter to allow direct injections into the infusion site, bypassing the controlled delivery system.

By physically separating the components of controlled drug delivery, each can be optimized for its function. The pump must store drugs for long periods of time and prevent degradation by chemical or bacterial action. The control unit must handle the drug safely but, due to the rapid throughput, avoidance of degradation is a lesser requirement. It has adjustable and calibrated parts that set up minimum and maximum flow rates. To accommodate a wide range of drug types, the control unit of the correct flow range is mated with the pump of the size needed. These components are heat sterilizable and care must be taken to eliminate any microorganisms that could live in the drug stored in the pump. The electronics package must contain batteries and other heat sensitive components that cannot be heat sterilized. Since the electronics package is separate from the pump and control unit, it can be sterilized by chemical means. After each has been separately sterilized, the electronics package and pump control unit are mated at the time of implantation.

It is apparent that many modifications and variations of this invention as hereinbefore set forth may be made without departing from the spirit and scope thereof. The specific embodiments described are given by way of example only and the invention is limited only by the terms of the appended claims.

WHAT IS CLAIMED IS:

1. An implantable magnetically controlled system for the infusion of drugs into an animal body from a pressure actuated drug delivery device, said system including a magnetically actuated valve comprising:

A) a body,

B) a shallow cavity within said body,

C) an inlet opening to one side of said cavity,

D) an outlet opening from the opposite side of said cavity,

E) a movable valving element positioned within said cavity to obstruct one of said openings,

F) a permanent armature magnet associated with said valving element, and

G) biasing means within said body to maintain said valving element in one of two positions relative to said obstructed opening.

2. A system according to claim 1 wherein said biasing means comprises at least one biasing magnetic means of equal or lesser field intensity associated with the valve body closely spaced from said armature magnet with magnetic axes aligned.

3. A system according to claim 2 wherein said biasing magnetic means is a permanent magnet.

4. A system according to claim 2 wherein said biasing magnetic means is a ferromagnetic shunt.

5. A system according to claim 2 wherein said biasing means comprises a pair of permanent biasing magnets of lesser field intensity associated with the valve body closely spaced from opposite sides of said armature

magnet with magnetic axes aligned and unlike poles adjacent.

6. A system according to claim 1 wherein said valving element comprises a hinged flap disk to which said armature magnet is attached.

7. A system according to claim 1 wherein:

A) said valving element is a flap disk within said cavity,

B) said armature magnet is attached to said disk,

C) said outlet opening is disposed at one side of the cavity underlying the edge of the disk,

D) a resilient O-ring is disposed around the outlet opening under the disk, and

E) said disk is hinged at the edge opposite from the outlet opening.

8. A system according to claim 7 wherein said biasing means are magnets disposed relative to the body to bias said valve disk in normally closed position.

9. A system according to claim 1 wherein:

A) a bypass passage extends through said body, and

B) said inlet opening is in direct fluid communication with said passage.

10. A system according to claim 9 wherein:

A) one end of said bypass passage is connected to a pressure actuated drug storage and delivery device,

B) the opposite end of said bypass passage is connected through a flow restrictor to a catheter for drug flow to the infusion site, and

C) said outlet opening is connected through a flow restrictor of lesser resistance to said catheter.

11. A system according to claim 1 wherein:

A) an electromagnetic coil is positioned on said body spaced from but within the field of said armature magnet, and

B) said coil is connected to an implantable power source through switch means for activating said coil.

12. A system according to claim 11 wherein said switch means includes a clock circuit for timing activation of said coil.

13. A system according to claim 1 wherein said body and valving elements are composed of inert, non-toxic biocompatible material.

14. A system according to claim 10 wherein said material is titanium.

15. A system according to claim 2 wherein said permanent magnets are samarium-cobalt.

AMENDED CLAIMS
(received by the International Bureau on 22 October 1980 (22.10.80))

1. An implantable magnetically controlled system for the infusion of drugs into an animal body from a pressure actuated drug delivery device, said system including a magnetically actuated valve comprising:

A) a body,

B) a shallow cavity within said body,

C) an inlet opening to one side of said cavity,

D) an outlet opening from the opposite side of said cavity,

E) a movable valving element positioned within said cavity to obstruct one of said openings,

F) a permanent armature magnet associated with said valving element, and

G) biasing means within said body to maintain said valving element in one of two positions relative to said obstructed opening.

2. A system according to claim 1 wherein said biasing means comprises at least one biasing magnetic means of equal or lesser field intensity associated with the valve body closely spaced from said armature magnet with magnetic axes aligned.

3. A system according to claim 2 wherein said biasing magnetic means is a permanent magnet.

4. A system according to claim 2 wherein said biasing magnetic means is a ferromagnetic shunt.

5. A system according to claim 2 wherein said biasing means comprises a pair of permanent biasing magnets of lesser field intensity associated with the valve body closely spaced from opposite sides of said armature

magnet with magnetic axes aligned and unlike poles adjacent.

6. A system according to claim 1 wherein said valving element comprises a hinged flap disk to which said armature magnet is attached.

7. A system according to claim 1 wherein:

A) said valving element is a flap disk within said cavity,

B) said armature magnet is attached to said disk,

C) said outlet opening is disposed at one side of the cavity underlying the edge of the disk,

D) a resilient O-ring is disposed around the outlet opening under the disk, and

E) said disk is hinged at the edge opposite from the outlet opening.

8. A system according to claim 7 wherein said biasing means are magnets disposed relative to the body to bias said valve disk in normally closed position.

9. A system according to claim 1 wherein:

A) a bypass passage extends through said body, and

B) said inlet opening is in direct fluid communication with said passage.

10. A system according to claim 9 wherein:

A) one end of said bypass passage is connected to a pressure actuated drug storage and delivery device,

B) the opposite end of said bypass passage is connected through a flow restrictor to a catheter for drug flow to the infusion site, and

C) said outlet opening is connected through a flow restrictor of lesser resistance to said catheter.

11. A system according to claim 1 wherein:

A) an electromagnetic coil is positioned on said body spaced from but within the field of said armature magnet, and

B) said coil is connected to an implantable power source through switch means for activating said coil.

12. A system according to claim 11 wherein said switch means includes a clock circuit for timing activation of said coil.

13. A system according to claim 1 wherein said body and valving elements are composed of inert, non-toxic biocompatible material.

14. A system according to claim 10 wherein said material is titanium.

15. A system according to claim 2 wherein said permanent magnets are samarium-cobalt.

(New) 16. A system for implantation in an animal body for the infusion of liquid drugs into said body, said system comprising:

A) a pressure actuated drug delivery device comprising:

1) a housing,

2) a collapsible drug chamber within the housing,

3) an inlet passage to said drug chamber,

4) a penetrable resilient stopper in that passage,

5) a propellant chamber within the housing surrounding the drug chamber, and

6) a liquid within the propellant chamber whose vapor pressure is such that, under conditions of normal body temperature, pressure is exerted upon the collapsible chamber; and

B) a magnetically actuated valve connected to the drug chamber of the drug delivery device and comprising:

1) a body,

2) a shallow cavity within said body,

3) an inlet opening to one side of said cavity, said inlet connected to receive drug from the drug chamber of the drug delivery device,

4) an outlet opening from the opposite side of said cavity,

5) a movable flap disk valving element positioned within said cavity to obstruct one of said openings,

6) a permanent armature magnet attached to said flap disk valving element, and

7) biasing means within said body to maintain said valving element in one of two positions relative to said obstructed opening.

(New) 17. A system according to claim 16 wherein said biasing means of the magnetically actuated valve comprises at least one biasing magnetic means of equal or lesser field intensity compared with said armature magnet associated with the valve body and disposed so as to be closely spaced from said armature magnet with the magnetic axes aligned.

(New) 18. A system according to claim 17 wherein said biasing means comprises a pair of permanent biasing magnets of lesser field intensity than said armature magnet associated with the valve body and disposed so as to be be closely spaced from opposite sides of said armature magnet with the magnetic axes aligned and unlike poles adjacent.

(New) 19. A system according to claim 16 wherein:

A) said outlet opening of the magnetically actuated valve is disposed at one side of the cavity underlying the surface adjacent to the edge of the flap disk,

B) a resilient O-ring is disposed around the outlet opening under the disk, and

C) said disk is hinged at the edge opposite from the outlet opening.

(New) 20. A system according to claim 16 wherein:

A) a bypass passage extends through said body of the magnetically actuated valve, and

B) said inlet opening of the valve is in direct fluid communication with said passage.

(New 21. A system according to claim 20 wherein:

A) one end of said bypass passage is connected to the pressure actuated drug delivery device,

B) the opposite end of said bypass passage is connected through a flow restrictor to a catheter for drug flow to the infusion site, and

C) said outlet opening is connected through a flow restrictor of lesser resistance to said catheter.

(New) 22. A system according to claim 16 wherein:

A) an electromagnetic coil is positioned on said body of the magnetically actuated valve spaced from but within the field of said armature magnet, and

B) said coil is connected to an implantable power source through switch means for activating said coil.

(New) 23. A system according to claim 22 wherein said switch means includes a clock circuit for timing activation of said coil.

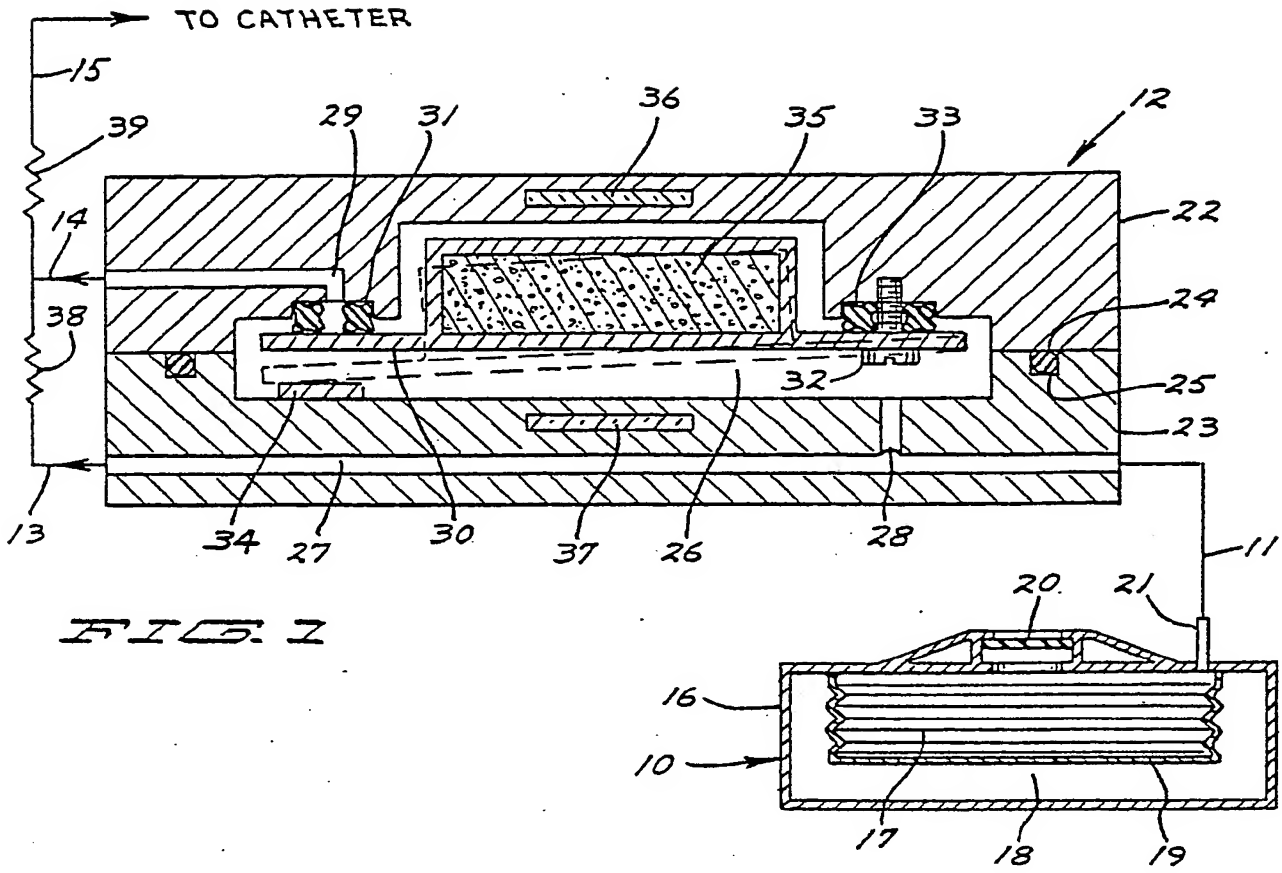


FIG. 1

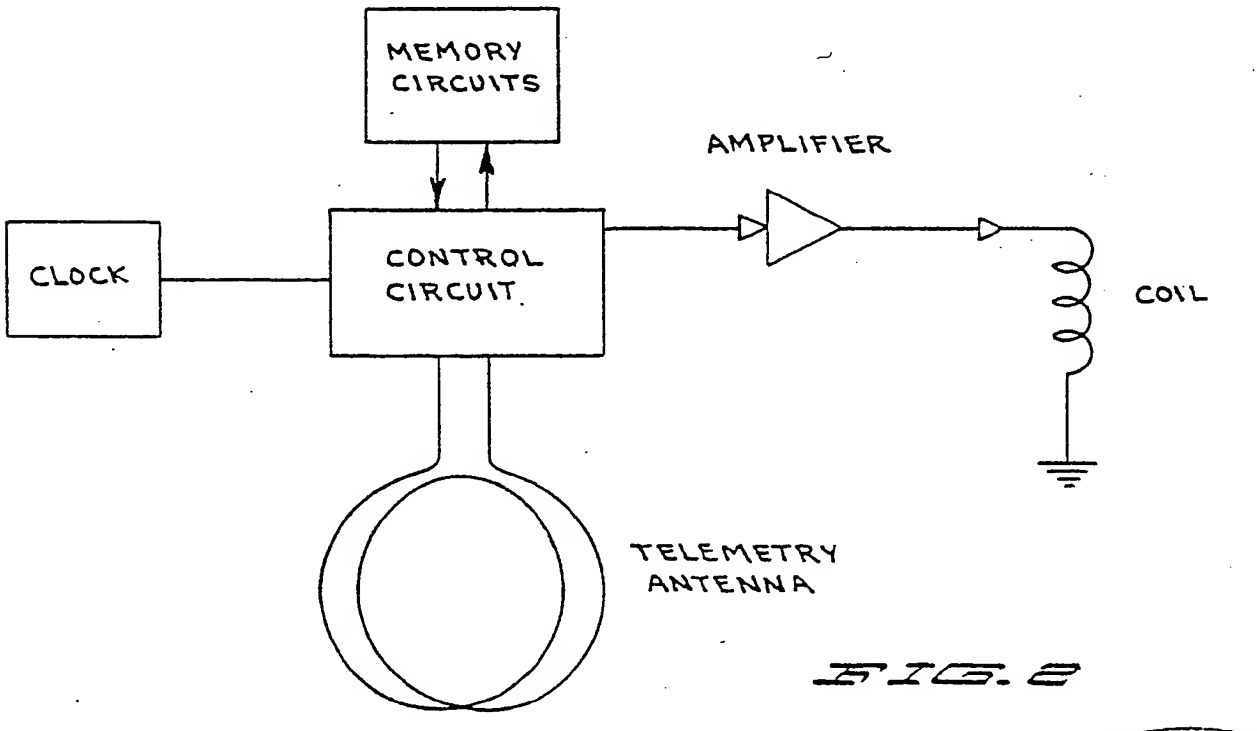
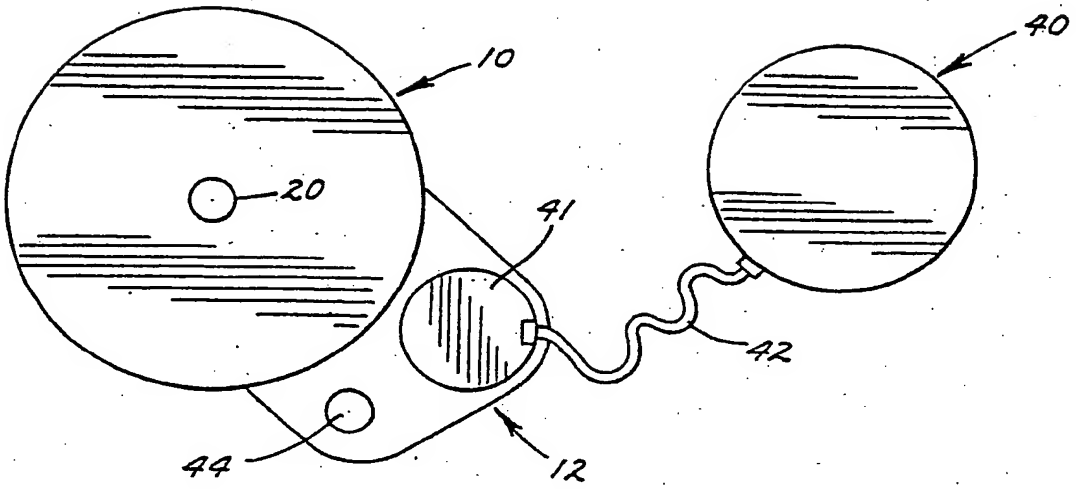


FIG. 2

FIG. 3



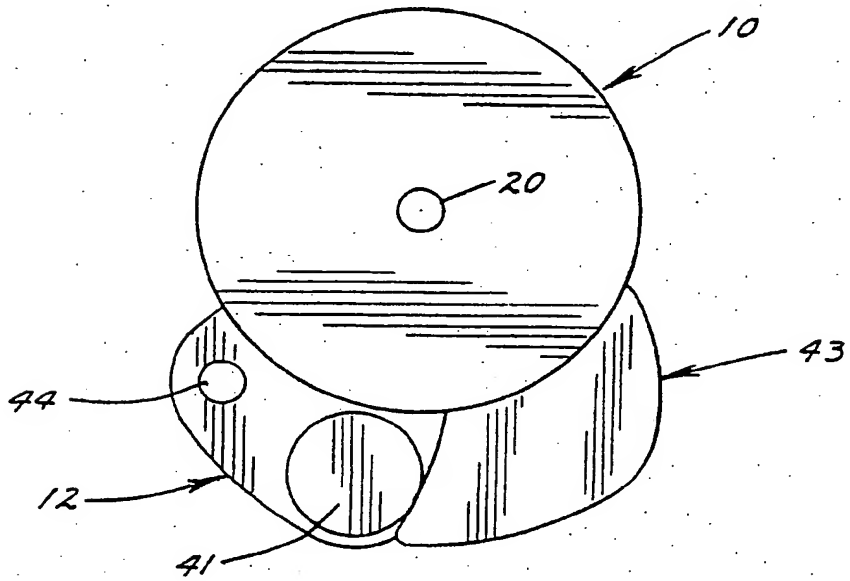


FIG. 4

INTERNATIONAL SEARCH REPORT

International Application No PCT/US80/00841

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [3]

According to International Patent Classification (IPC) or to both National Classification and IPC

INT. CL.[3] A61M 1/00, F16K 31/08
U.S. CL. 128/214F,274; 251/65,141

II. FIELDS SEARCHED

Minimum Documentation Searched [4]

Classification System	Classification Symbols
U.S.	128/213R, 214F,260,274,DIGEST 12; 251/65,141

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [5]

TRANSACTIONS OF THE AMERICAN SOCIETY FOR ARTIFICIAL INTERNAL ORGANS, 1970-1978.

III. DOCUMENTS CONSIDERED TO BE RELEVANT [14]

Category *	Citation of Document, [16] with indication, where appropriate, of the relevant passages [17]	Relevant to Claim No. [18]
X	US,A, 3,270,763, PUBLISHED 06 SEPTEMBER 1966, KIEFER.	1-5,9-15
X	US,A, 2,575,086, PUBLISHED 13 NOVEMBER 1951, ATCHISON.	1-5,9-15
X	US,A, 2,736,331, PUBLISHED 28 FEBRUARY 1956, SEELER.	1-4,6-8,15
X	N, TRANSACTIONS OF THE AMERICAN SOCIETY FOR ARTIFICIAL INTERNAL ORGANS, VOLUME 14, ISSUED 27 APRIL 1978, P.R. PERKINS ET AL, DESIGN AND INITIAL TESTING OF A TOTALLY IMPLANTABLE TRANSCUTANEOUSLY CONTROLLABLE INSULIN DELIVERY DEVICE, PAGES 229-231.	9-12,14
X	US,A, 3,570,806, PUBLISHED 16 MARCH 1971, STURMAN ET AL.	7,8
X	US,A, 2,310,562, PUBLISHED 09 FEBRUARY 1943, WHITTINGTON.	11,12
X	US,A, 3,890,968, PUBLISHED 24 JUNE 1975, PIERCE ET AL.	11,12

* Special categories of cited documents: [15]

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"L" document cited for special reason other than those referred to in the other categories
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but on or after the priority date claimed
"T" later document published on or after the international filing date or priority date and not in conflict with the application, but cited to understand the principle or theory underlying the invention
"X" document of particular relevance

IV. CERTIFICATION

Date of the Actual Completion of the International Search [2]	Date of Mailing of this International Search Report [2]
22 SEPTEMBER 1980	29 SEP 1980
International Searching Authority [1]	**Signature of Authorized Officer [20]**
ISA/US	David R. Sadowski DAVID R. SADOWSKI

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

X	N, DIABETES, VOLUME 28, ISSUED JULY 1979, B.J. BLACKSHEAR ET AL, CONTROL OF BLOOD GLUCOSE IN EXPERIMENTAL DIABETES BY MEANS OF A TOTALLY IMPLANTABLE INSULIN INFUSION DEVICE, PAGES 634-638.	13,14
X	N, CHEMICAL ENGINEER'S HANDBOOK, FIFTH EDITION, R.H. PERRY, 1973, McGRAW-HILL BOOK CO., PAGE 23-60.	13,14
A	US,A, 3,731,681, PUBLISHED 08 MAY 1973, BLACKSHEAR ET AL.	1-15

V. ☐ OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE [10]

This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. ☐ Claim numbers _____, because they relate to subject matter [12] not required to be searched by this Authority, namely:

2. ☐ Claim numbers _____, because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out [13], specifically:

VI. ☐ OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING [11]

This International Searching Authority found multiple inventions in this international application as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.

2. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:

3. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:

Remark on Protest

☐ The additional search fees were accompanied by applicant's protest.

☐ No protest accompanied the payment of additional search fees.